Complete Summary

GUIDELINE TITLE

American Gastroenterological Association medical position statement: nonalcoholic fatty liver disease.

BIBLIOGRAPHIC SOURCE(S)

American Gastroenterological Association medical position statement: nonalcoholic fatty liver disease. Gastroenterology 2002 Nov;123(5):1702-4. [3 references] PubMed

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Nonalcoholic fatty liver disease (NAFLD)

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Risk Assessment
Treatment

CLINICAL SPECIALTY

Family Practice
Gastroenterology
Internal Medicine
Nutrition

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To present recommendations for the diagnosis and treatment of nonalcoholic fatty liver disease (NAFLD) with the intention of assisting physicians in making patient care decisions

TARGET POPULATION

- Adults and children that may have risk factors for nonalcoholic fatty liver disease (NAFLD)
- Adults and children with suspected or confirmed nonalcoholic fatty liver disease

INTERVENTIONS AND PRACTICES CONSIDERED

Risk Assessment/Prognosis

1. Assessment of risk factors for nonalcoholic fatty liver disease (NAFLD)
2. Evaluation of prognosis in patients with established nonalcoholic fatty liver disease, including laboratory evaluation of serum bilirubin and albumin levels as well as prothrombin time and liver biopsy

Diagnosis

1. Laboratory evaluation:
    - Measurement of biochemical markers of liver injury and cholestasis, including serum aspartate aminotransferase, alanine aminotransferase, and alkaline phosphatase levels
    - Measurement of liver functions, including serum bilirubin, albumin, and prothrombin time
2. Assessment for alternative or coexisting clinical conditions (e.g., hepatitis C) using the relevant laboratory testing
3. Assessment of alcohol consumption (detailed clinical evaluation, including interview of family members in some cases, and assessment of the aspartate aminotransferase/alanine aminotransferase ratio)
4. Imaging of liver by sonography, computerized tomography scan, or magnetic resonance imaging
5. Liver biopsy

Management/Treatment

1. Weight management strategies: counseling regarding caloric and fat restriction and exercise; gastric bypass, as indicated
2. Monitoring: signs of subacute nonalcoholic steatohepatitis during weight loss; liver function checked at intervals depending on the rapidity of weight loss
3. Vitamin E
4. Ursodeoxycholic acid

5. Pharmacologic agents that decrease insulin resistance

Note: Guideline developers considered, but did not recommend, pharmacologic agents to induce weight loss in patients with nonalcoholic fatty liver disease.

MAJOR OUTCOMES CONSIDERED

- Sensitivities, specificities, predictive values, risks, and costs associated with diagnostic measures
- Effect of treatment on liver histology and alanine aminotransferase (ALT) levels
- Health outcomes (cirrhosis, death, liver-related death) for various histologic patterns of nonalcoholic fatty liver disease (NAFLD)

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The technical review supporting the guideline recommendations is based on the following: (1) a formal review and analysis of the literature on nonalcoholic fatty liver disease (NAFLD) (Index Medicus, 1950–1966; MEDLINE, 1966–2001), (2) several published guidelines and meta-analyses, including the American Gastroenterological Association's policy statement on guidelines, (3) the Manual for Guideline Development (American Gastroenterological Association: Clinical Practice and Practice Economics Committee) as well as the policy statement on the development and use of practice guidelines of the American Association for the Study of Liver Diseases, and (4) 12 years of experience on the part of the author of the technical review in managing patients with liver diseases. There is a paucity of controlled data (types I and II as defined by the National Health Service [NHS] Center for Reviews and Dissemination) on nonalcoholic fatty liver disease. The technical report summarizes the published literature and includes reported case series and case reports. Letters and abstracts have been included only when they represent the only literature in a given area or have been cited frequently in existing literature.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence used by the American Gastroenterological Association (AGA)

I: Well-designed randomized controlled trials

II-1a: Well-designed controlled trials with pseudo-randomization

II-1b: Well-designed controlled trials with no randomization

II-2a: Well-designed cohort (prospective) study with concurrent controls

II-2b: Well-designed cohort (prospective) study with historical controls

II-2c: Well-designed cohort (retrospective) study with concurrent controls

II-3: Well-designed case-control (retrospective) study

III: Large differences from comparisons between times and/or places with and without intervention (in some instances, these may be equivalent to level II or I)

IV: Opinions of respected authorities based on clinical experience, descriptive studies, and reports of expert panels

Levels of Evidence used by the American Association for the Study of Liver Diseases

Grade/Definition

I: Evidence from multiple well-designed randomized controlled trials, each involving a number of participants to be of sufficient statistical power

II: Evidence from at least one large well-designed clinical trial with or without randomization from cohort or case-control analytic studies or well-designed meta-analyses

III: Evidence based on clinical experience, descriptive studies, or reports of expert committees

IV: Not rated

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Categories Reflecting the Evidence to Support the Use of a Guideline Recommendation by the American Association for the Study of Liver Diseases (AASLD)

Category/Definition

A: Survival benefit

B: Improved diagnosis

C: Improvement in quality of life

D: Relevant pathophysiologic parameters improved

E: Impacts cost of health care

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The American Gastroenterological Association (AGA) Clinical Practice Committee approved this guideline on March 3, 2002. The American Gastroenterological Association Governing Board approved it on May 19, 2002. The American Association for the Study of Liver Diseases (AASLD) Governing Board and the American Association for the Study of Liver Diseases Practice Guidelines Committee approved it on May 24, 2002.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The levels of evidence for the American Gastroenterological Association (AGA) (I, II-1a, II-1b, II-2a, II-2b, II-2c, II-3, III, IV), the categories by the American Association for the Study of Liver Diseases (AASLD) that reflect the evidence to support the use of a guideline recommendation (A-E), and the levels of evidence for the AASLD (I-IV) are repeated at the end of the Major Recommendations field.

Definition

Nonalcoholic fatty liver disease (NAFLD) represents a spectrum of disorders characterized by predominantly macrovesicular hepatic steatosis that occur in individuals even in the absence of consumption of alcohol in amounts considered harmful to the liver.

When Should the Presence of NAFLD Be Suspected?

The presence of underlying NAFLD should be considered in those who have risk factors for this condition. Such risk factors include obesity, diabetes, hypertriglyceridemia, severe weight loss (especially in those who were obese initially), and specific syndromes associated with insulin resistance (e.g., lipoatrophic diabetes) (refer to the original guideline document, Table 4, Conditions Associated With Steatohepatitis).

NAFLD should also be considered in the differential diagnosis of elevated serum aminotransferase levels in individuals who are receiving drugs known to be associated with NAFLD. Finally, the presence of NAFLD should also be considered in those with persistent elevation of serum alanine aminotransferase levels for which another cause cannot be found.

Recommendation category: AGA: III and IV; AASLD: B, III

Evaluation of a Patient With Suspected NAFLD

Clinical and Laboratory Evaluation

The initial clinical and laboratory assessment of a patient with suspected NAFLD should be determined by the specific clinical circumstances in an individual case (refer to the original guideline document, Figure 1, Evaluation of NAFLD). Serum aspartate aminotransferase, alanine aminotransferase, and alkaline phosphatase levels (biochemical markers of liver injury and cholestasis) and liver functions (serum bilirubin, albumin, and prothrombin time) should be measured (step 1). The presence of alternative or coexisting clinical conditions (e.g., hepatitis C) should be assessed using the relevant laboratory test (step 2). An attempt to estimate the extent of underlying alcohol consumption should be made (step 3). This usually involves a detailed clinical evaluation, including interview of family members in some cases, and assessment of the aspartate aminotransferase/alanine aminotransferase ratio. In the absence of cirrhosis, when the aspartate aminotransferase/alanine aminotransferase ratio exceeds 2, the diagnosis of alcoholic liver disease may be made with greater confidence.

Recommendation category: AGA: III and IV; AASLD: B, III

Confirmation of Fatty Liver Disease

Once ongoing alcohol use (>20–30 g/day) and other common causes of liver disease are excluded by clinical and laboratory evaluation, the liver is usually imaged by sonography, computerized tomography scan, or magnetic resonance imaging (step 4). These modalities can be used to determine the presence of biliary tract disease and focal liver disease, which may be responsible for elevation of liver enzyme levels. However, they do not distinguish between fatty liver,

steatohepatitis, and steatohepatitis with fibrosis and therefore cannot be used to make these distinctions. Although sonography is slightly more sensitive, computerized tomography scan is more specific but more expensive. Sufficient data on the comparative assessment of these tests, including their cost and predictive values, on which to base a recommendation are lacking. Hence, a recommendation about the use of one modality versus another cannot be made at this time. It is, however, common practice to use either sonography or computerized tomography scan.

Recommendation category: AGA: II, III, IV; AASLD: B, II, III

The diagnosis of steatohepatitis, as opposed to fatty liver alone, and its grade and stage can only be made with precision by a liver biopsy. The decision to perform a biopsy usually involves assessment of the specific clinical circumstances in a given individual with suspected NAFLD (step 5). The cost and risks of the biopsy are generally weighed against the value of the information obtained from the biopsy in estimating prognosis and guiding future management decisions. If a decision is made not to perform a biopsy, it is advisable to discuss the potential implications with the patient.

Recommendation category: AGA: II, III, IV; AASLD: B, II, III

Evaluation of Prognosis

The prognosis of NAFLD requires assessment of the stage of the disease and the degree of liver dysfunction. Liver function is generally assessed from the serum bilirubin and albumin levels as well as prothrombin time. These usually do not become abnormal unless there is underlying cirrhosis or rapid severe weight loss. Increasing age and body weight as well as diabetes are risk factors for increased hepatic fibrosis. However, the stage of the disease can only be ascertained by a liver biopsy. The decision to perform a liver biopsy to assess the stage of the disease should be weighed against the risks of the biopsy and the impact of the information obtained from the biopsy on future management decisions. If a decision is made not to perform a biopsy, it is advisable to discuss the implications of the decision with the patient.

Recommendation category: AGA: II, III, IV; AASLD: B, II, III

Treatment of NAFLD

Those who are overweight (body mass index >25 kg/m^2) and have NAFLD should be considered for a weight loss program. A target of 10% of baseline weight is often used as an initial goal of weight loss. Weight loss should proceed at a rate of 1–2 lb/wk. Dietary recommendations generally include both caloric restriction and a decrease in saturated fats as well as total fats to <30% or less of total calories. Although there are no data to support or refute the value of decreasing saturated fats and increasing the fiber content of diet on NAFLD, it is our belief that these interventions may be of value. However, further research is needed to substantiate this opinion. Diet modifications are usually accompanied by a recommendation to exercise regularly. Both intermittent as well as daily exercise can help achieve weight loss and improve insulin sensitivity. The role of pharmacologic agents to induce weight loss in patients with NAFLD has not been

studied. Therefore, no recommendation about their safety or efficacy in the management of NAFLD can be made at this time. Those with a body mass index >35 kg/m^2 and NAFLD may be considered for more aggressive weight management, including a gastric bypass. The decision to perform this surgery should take into consideration the morbidity and mortality associated with the procedure as well as the risk of developing subacute nonalcoholic steatohepatitis and liver failure during rapid weight loss. Patients should be monitored for signs of subacute nonalcoholic steatohepatitis during weight loss and liver function checked at intervals depending on the rapidity of weight loss.

Recommendation category: AGA: III, IV; AASLD: D, III

In diabetic individuals, hemoglobin A_{1c} should ideally be brought to <7%. However, the impact of this on NAFLD is not established. There is no specific pharmacologic treatment that has been shown to be effective in the treatment of NAFLD. The clinical alternatives available include vitamin E, ursodeoxycholic acid, and pharmacologic agents that decrease insulin resistance. Although it is common practice to use either vitamin E or ursodeoxycholic acid, there are no data clearly showing their efficacy or comparing the utility of these 2 drugs.

Recommendation category: AGA: IV; AASLD: D, III

Definitions:

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Categories Reflecting the Evidence to Support the Use of a Guideline Recommendation by the American Association for the Study of Liver Diseases (AASLD)

Category/Definition

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B: Improved diagnosis

C: Improvement in quality of life

D: Relevant pathophysiologic parameters improved

E: Impacts cost of health care

Levels of Evidence used by the American Association for the Study of Liver Diseases

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III: Evidence based on clinical experience, descriptive studies, or reports of expert committees

IV: Not rated

CLINICAL ALGORITHM(S)

The original guideline contains a clinical algorithm for the evaluation of nonalcoholic fatty liver disease (NAFLD).

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Identification of patients at risk for nonalcoholic fatty liver disease (NAFLD)
- Appropriate selection of diagnostic and therapeutic measures for patients with suspected or confirmed nonalcoholic fatty liver disease

- Correction of the risk factors for nonalcoholic steatohepatitis (i.e., insulin resistance, decreasing delivery of fatty acids to the liver, and use of drugs with potentially hepatoprotective effects)
- Improved health outcomes for patients with nonalcoholic fatty liver disease

POTENTIAL HARMS

- Costs and risks associated with liver biopsy
- Morbidity and mortality associated with gastric bypass
- Risk of developing subacute nonalcoholic steatohepatitis and liver failure during rapid weight loss

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

The guidelines are intended to be flexible, in contrast to "standards of care," which are inflexible policies to be followed in almost every case. Thus, although the recommendation should be followed in most cases, the decision to do so is up to the physician based on the circumstances of the individual case.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

American Gastroenterological Association medical position statement: nonalcoholic fatty liver disease. Gastroenterology 2002 Nov;123(5):1702-4. [3 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2002 Nov

GUIDELINE DEVELOPER(S)

American Association for the Study of Liver Diseases - Private Nonprofit Research Organization
American Gastroenterological Association - Medical Specialty Society

SOURCE(S) OF FUNDING

American Gastroenterological Association
American Association for the Study of Liver Diseases

GUIDELINE COMMITTEE

American Gastroenterological Association Clinical Practice Committee
American Association for the Study of Liver Diseases Practice Guidelines Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Not stated

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

According to the guideline developer, the Clinical Practice Committee meets three times a year to review all American Gastroenterological Association guidelines. This review includes new literature searches of electronic databases followed by expert committee review of new evidence that has emerged since the original publication date.

GUIDELINE AVAILABILITY

Electronic copies: Available from the American Gastroenterological Association (AGA) Gastroenterology journal Web site.

Print copies: Available from the American Gastroenterological Association, 4930 Del Ray Avenue, Bethesda, MD 20814.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- A. J. Sanyal. AGA technical review on nonalcoholic fatty liver disease. Gastroenterology 2002 Nov;123(5):1705-25.

Electronic copies: Available from the American Gastroenterological Association (AGA) Gastroenterology journal Web site.

Print copies: Available from the American Gastroenterological Association, 4930 Del Ray Avenue, Bethesda, MD 20814.

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on January 14, 2003. It was verified by the guideline developer on February 27, 2003.

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